

Amendments to the Specification:

Please replace the paragraph beginning at page 20, line 1, with the following rewritten paragraph:

--Network architecture. For all neural network experiments, the Stuttgart Neural Network Simulator (SNNS) was used. A. Zell et al., Recent Developments of the SNNS Neural Network Simulator, Aerospace Sensing Int'l Symp. 708-719 (Orlando, Florida, SPIE 1991) (~~http://www-ra.informatik.uni-tuebingen.de/SNNS/~~) (www-ra.informatik.uni-tuebingen.de/SNNS/). The system comprises a kernel, batch language, and graphical interface. Initial experiments were usually carried out with the graphical interface followed by more thorough cross-validation testing utilizing the kernel, batch language, and custom PERL scripts.--

Please replace the paragraph beginning at page 20, line 15, with the following rewritten paragraph:

--Various supervised learning algorithms provided by SNNS were tested on the problem, but the majority of experiments were performed using the back-propagation (backprop) algorithm with a momentum term. D.E. Rumelhart et al., Learning Internal Representations by Error Propagation, 1 Parallel Distributed Processing: Foundations 318-364 (MIT Press 1986). The back-propagation method performs connection weight adjustments to

minimize the difference between the training signal and the actual network output at the output nodes. It is a gradient-descent method that recursively adjusts weights to reduce the error of the network's output for a given input pattern. The rate of descent is controlled by the learning parameter η . In the back-propagation momentum method, the learning equation utilizes two additional parameters, μ and c , to reduce oscillation during learning and avoid flat spots in the error space. Experiments indicated that the back-propagation momentum method generalized better than the basic back-propagation method (without a momentum term).--

Please replace the paragraph beginning at page 25, line 8, with the following rewritten paragraph:

--Training methods. The system has a single output unit, corresponding to the activity of the ODN. There are choices available about whether the output node is trained directly with the continuous-valued activities measured in a lab, or a secondary function thereof. Experiments training the output node directly with measured activity were not the best at generalizing. So other training functions were tested. Both a binary threshold function with a cutoff of 0.25 and a 3-way threshold were tested. In general, the binary threshold function will have a cutoff in the range of about 0.01-0.50. The 3-way threshold is given by:

$$o = \begin{cases} 0, & act \leq 0.25 \\ 0.25, & 0.25 < act \leq 0.5 \\ 1.0, & act > 0.5 \end{cases}. \quad (6)$$

Please replace the paragraph beginning at page 26, line 19, with the following rewritten paragraph:

--Combination approaches. Several approaches were tested wherein the predictions of multiple networks were combined or the predictions of network(s) with other methods were combined. The simplest approach, which is in essence a "voting" scheme, averages the outputs of several selected networks when a single "ODN sequence" is presented to each of them. Another approach to combining several predictors is logistic regression. D.W. Hosmer, *Applied Logistic Regression* (Wiley 1989); ~~<http://m2.aol.com/johnp71/logistic.html>~~ m2.aol.com/johnp71/logistic.html. This is a process where a logistic transform equation is used in combination with a linear regression of the transformed data to provide a probability estimator based on a set of independent variables. In fact, this process can be used directly for activity prediction with the motif counts as the independent variables. Matveeva et al., *supra*,

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explored this possibility. The downside of this approach is the difficulty of analytically maximizing the likelihood estimator over such a large set of independent variables (all motifs, or a large portion thereof). The algorithms tested demonstrated some instability, particularly for those motifs for which there are few or no examples.--